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Role of growth hormone in the amino acid–induced acute rise in renal function in man

RAIMUND HIRSCHBERG and JOEL D. KOPPLE

Division of Nephrology and Hypertension, Harbor–UCLA Medical Center, Torrance, California, USA

Role of growth hormone in the amino acid–induced acute rise in renal function in man. To examine whether plasma growth hormone is necessary for the amino acid–induced rise in effective renal plasma flow (ERPF, PAH clearance) and GFR (inulin clearance), arginine HCl, 500 mg/kg, was infused for 30 minutes into eight normal and six growth hormone–deficient individuals. During infusion, ERPF increased in the normal and growth hormone–deficient subjects by 28.9 ± 11.4 SD-% ($P < 0.01$) and 46.5 ± 14.4% ($P < 0.001$). GFR rose by 23.7 ± 5.9% ($P < 0.05$) and 42.7 ± 29.1% ($P < 0.001$) in the two groups. Plasma growth hormone rose only in the normal subjects, while glucagon increased in both groups. Infusion of arginine HCl, 200 mg/kg, into normals increased ERPF and GFR without increasing plasma osmolality. Lower arginine doses essentially did not affect ERPF, GFR, growth hormone, or glucagon. Infusion of D-glucose into normals raised plasma osmolality as high as with arginine HCl, 500 mg/kg, but increased ERPF only slightly and not GFR; D-glucose infusion caused a delayed rise in growth hormone that was unassociated with an increase in ERPF or GFR. An infusion of ammonium chloride with sodium chloride, which provided an amount of chloride similar to the 500 mg/kg arginine HCl dose, did not change ERPF and GFR; this suggests that the chloride load did not cause the altered renal hemodynamics stimulated by arginine HCl. These findings indicate that neither normal plasma growth hormone levels nor a rise in growth hormone mediates the arginine–induced acute increase in ERPF or GFR. This effect is also not due to the osmolar load but could be caused by the rise in plasma glucagon.

Humans and animals undergo a transient but reproducible increase in renal plasma flow (RPF) and glomerular filtration rate (GFR) in response to an amino acid or protein load [1–4]. Although several studies have examined the mechanisms underlying this response, the factors controlling these processes are still not well defined. Growth hormone has been implicated as a possible cause of the amino acid or protein induced rise in RPF and GFR. The evidence stated briefly is as follows: (a) plasma growth hormone rises rapidly but transiently in response to a protein or amino acid load [5]; (b) injections of growth hormone for several days increases RPF and GFR in humans [6, 7]; (c) acromegaly, a disease with chronically–elevated plasma growth hormone concentrations, is also associated with high RPF and GFR [8]; (d) a protein meal increases GFR in normal individuals but not in growth hormone–deficient patients [9].

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The present study was undertaken to examine in greater detail whether the presence of normal plasma growth hormone levels or a rise in plasma growth hormone is necessary for the amino acid–induced rise in RPF and GFR. The question was addressed by infusing intravenously arginine hydrochloride, a potent secretagogue for growth hormone, into normal individuals and patients with growth hormone deficiency.

Methods

Studies were carried out in six patients with growth hormone deficiency and 27 normal individuals who were subjected to one or more of the following infusion protocols: Three men and three women with growth hormone deficiency, aged 33 ± 7 (SD) years, and four male and four female normal volunteers, aged 30 ± 5 years, were infused for 30 minutes with arginine HCl, 500 mg/kg body weight or 30 g, whichever was less. Their weights were 67.7 ± 1.4 and 62.9 ± 5.0 kg, respectively. Three men and one woman, 35 ± 6 years old, and all normal, received 200 mg/kg of arginine. Three normal men, 26 ± 4 years old, received 50 mg/kg arginine HCl; two men and one woman, normal, and 29 ± 3 years old, were given 10 mg/kg of arginine HCl and three male and two female normal volunteers, 32 ± 5 years old, received 1000 mg/kg of D-glucose monohydrate. This latter compound was infused as 5 ml/kg of 20% dextrose (900 mg/kg of anhydrous glucose) up to a maximum of 300 ml of the dextrose solution. Finally, five normal men, 33 ± 4 years old, were infused with 70 mmol of ammonium chloride and 70 mmol of sodium chloride in 300 ml water over 30 minutes.

The subjects showed no evidence of disease except for the endocrine disorders in the growth hormone–deficient patients. The causes of growth hormone deficiency were hereditary isolated growth hormone deficiency (one patient), hereditary panhypopituitarism (one patient), secondary panhypopituitarism due to Sheehan's syndrome (two patients), and hypophysectomy for nonmalignant tumors (two patients). The growth hormone–deficient patients received replacement therapy with thyroid (five subjects), testosterone (three patients),and prednisone (three subjects). Only two of the six patients had received growth hormone injections, but not for at least seven years before the study.

The subjects were fasted from midnight before the experiment until the study was completed. The only exception was water. The individuals drank 1000 ml of deionized water between 7:20 and 8:00 a.m. and 300 ml of deionized water every hour thereafter at exactly ten minutes before the hour. At 8:00

a.m. inulin (American Critical Care, McGaw Park, Illinois), 60 mg/kg of body weight, and para-aminohippuric acid (PAH, Merck, Sharp and Dohme, West Point, Pennsylvania, USA), 8 mg/kg body weight, were injected intravenously. This was followed by a continuous infusion of inulin, 0.5 mg/kg/min, and PAH, 0.25 mg/kg/min, in normal saline, at 31 ml/hr which lasted until 3:30 p.m. After one hour for equilibration, subjects began 14 clearance periods of 30 minutes each. Blood was drawn at the beginning and end of each clearance period to measure plasma inulin, PAH, sodium, osmolality and arginine. Between 11:30 a.m. and 12:00 noon, individuals received an infusion of 10% arginine HCl (R-Gene, Cutter Lab, Berkeley, California, USA) or 20% dextrose in water as discussed above. The 10% arginine HCl solution used in this study contained no potassium or sodium, and the osmolality of the infusate was measured in our laboratory to be 801 mOsm/kg. Immediately before and every 15 to 30 minutes after the onset of the arginine or dextrose infusion, blood was taken for plasma growth hormone and glucagon levels.

The ammonium chloride and sodium chloride solution was also infused from 11:30 a.m. to 12:00 noon. However, the protocol differed with the latter infusion in that only seven, 30 minute PAH and inulin clearances were performed; three before, one during and three after the infusion. Also, growth hormone, glucagon, sodium and arginine were not measured.

Effective renal plasma flow (ERPF) and glomerular filtration rate (GFR) were measured as the PAH and inulin clearances, respectively. Plasma PAH and inulin at the beginning and end of each clearance period were averaged for calculation of the clearance values. PAH and inulin were measured in plasma and urine as previously described [10, 11]. Two specimens were obtained at each blood drawing for measurement of PAH and inulin concentrations; each specimen was analyzed in duplicate or triplicate. A pooled control sample of plasma was measured with each batch of inulin and PAH determinations. The coefficients of variation for the analyses of the pooled controls were 2.9% for PAH and 4.3% for inulin. Sodium was measured in plasma and urine with a flame photometer (Model 143, Instrumentation Laboratory, Boston, Massachusetts, USA). Plasma osmolality was determined by freezing point depression (Microosmette Model 5004, Precision Systems, Sudbury, Massachusetts, USA).

Plasma human growth hormone was measured by radioimmunoassay in the Harbor-UCLA Clinical Research Center Laboratory using rabbit anti-human growth hormone antiserum. Plasma glucagon was measured by radioimmunoassay in the laboratory of Dr. Seymur Levin. Plasma arginine was measured with an automated amino acid analyzer, Model 121 MB (Beckman Instruments, Fullerton, California, USA). In subjects who received the glucose infusion, plasma glucose was measured with a glucose analyzer (Beckman Instruments). Data were analyzed by analysis of variance (when multiple baseline measurements were obtained) or by Student's or unpaired *t*-test. Results are presented as means and standard deviations.

Results

The plasma arginine concentrations during and after the arginine infusions are shown in Figure 1. In the normal subjects, there was a direct relation between the quantity of arginine infused, expressed per kg body weight, and the maximum rise

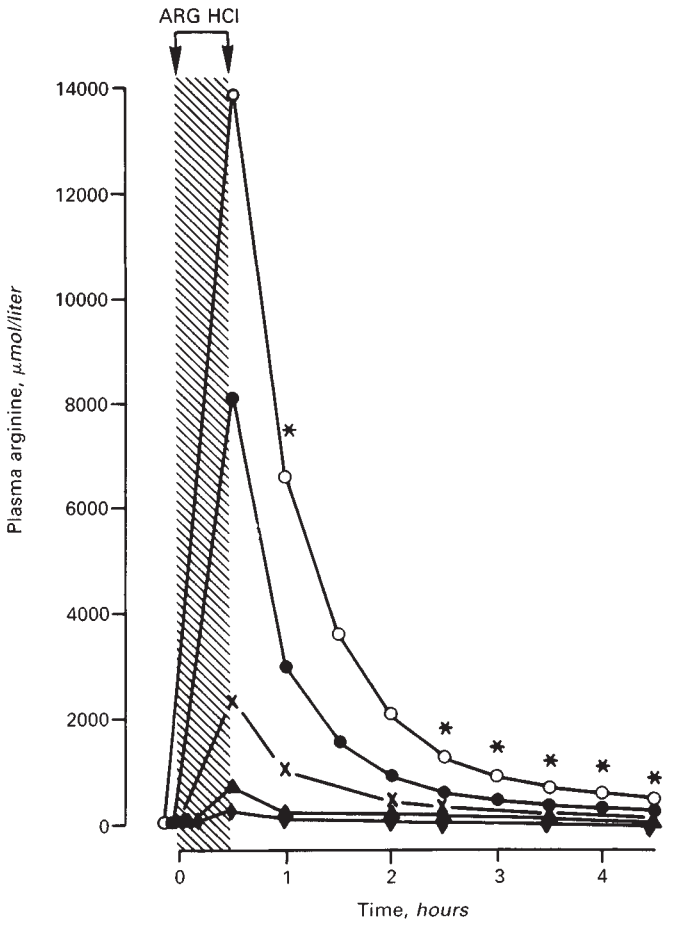

Fig. 1. *Mean plasma arginine concentrations before, during and after arginine HCl infusion in growth hormone deficient (GH DEF) patients and normal subjects infused with varying doses of arginine HCl.* The shaded bar indicates the time of infusion. The asterisks indicate a significant difference ($P < 0.05$) between the growth hormone deficient and normal subjects infused with 500 mg/kg of arginine HCl. Symbols are: (○) GH DEF, 500 mg/kg; (●) normal, 500 mg/kg; (X) normal, 200 mg/kg; (▲) normal, 50 mg/kg; (◆) normal, 10 mg/kg.

in arginine level ($r = 0.802$, $P < 0.05$). The maximum increase in plasma arginine in the growth hormone–deficient patients was not significantly greater than in the normal individuals who received 500 mg arginine HCl/kg. However, the plasma arginine concentrations were greater in the growth hormone deficient patients as compared to the latter individuals at 60 minutes, and 2.5 to 4.5 hours after the arginine infusion (Fig. 1). The actual intake of arginine HCl in the growth hormone deficient and normal subjects was 439 ± 95 and 450 ± 66 mg/kg, respectively.

The ERPF, GFR, and plasma growth hormone and glucagon levels are shown in Figure 2 and Table 1. For ERPF, GFR, and the fractional excretion of sodium, the baseline period for each patient is defined as the mean of the four clearance periods immediately prior to the infusion of arginine or glucose. During the baseline period, these parameters did not change.

In the normal and growth hormone–deficient subjects receiving arginine HCl, 500 mg/kg, there was a significant increase in ERPF of 28.9 ± 11.4% ($P < 0.01$) and 46.5 ± 14.4% ($P < 0.001$), respectively. Although the maximal ERPF levels did not differ

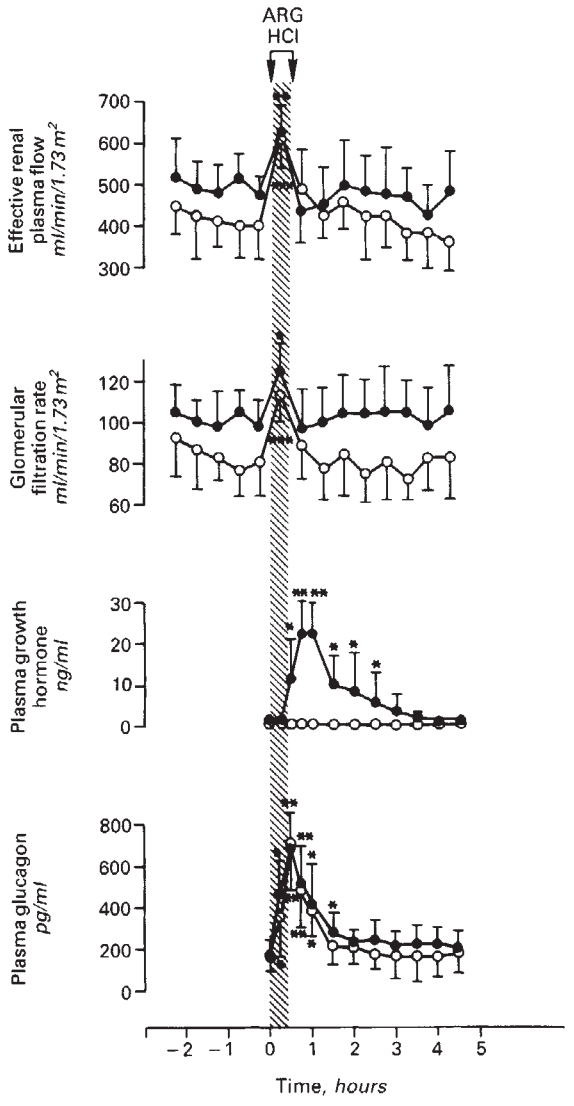

Fig. 2. *ERPF, GFR, plasma growth hormone and plasma glucagon in response to an infusion of arginine HCl in growth hormone deficient (○, 500 mg/kg) and normal subjects (●, 500 mg/kg).* The shaded bar indicates the period of the arginine HCl infusion. Significantly greater than the subjects' baseline or pre-infusion values: $*P < 0.05$, $**P < 0.01$, $***P < 0.001$.

between the two groups, the magnitude of the rise, expressed in absolute values or as a percent change was significantly greater in the growth hormone–deficient patients ($P < 0.05$). In both, the normal and growth hormone–deficient individuals, there was a significant rise in GFR during the arginine infusion of 23.7 ± 5.9% ($P < 0.05$) and 42.7 ± 29.1% ($P < 0.001$), respectively. This rise in GFR whether expressed in absolute values or as a percent increase, did not differ significantly between the two groups. In the individuals receiving 200 mg/kg of arginine HCl, the rise in ERPF and GFR was not different from the normal subjects infused with arginine HCl, 500 mg/kg (Table 1). The rise in ERPF and GFR in these three groups was rapid, reaching maximum levels during the arginine infusion and falling back to baseline during the 30 or 60 minute period that followed the infusion. There was no significant rise in ERPF or GFR in the normal subjects who received 50 or 10 mg/kg of arginine HCl.

During the arginine infusion, plasma growth hormone did not rise in the growth hormone–deficient patients. In the normal subjects receiving 500 or 200 mg/kg of arginine HCl plasma growth hormone was not increased after 15 minutes of the infusion, but was significantly elevated at the end of the infusion and attained maximum levels at 45 and 60 minutes after the onset of the arginine administration (Fig. 2 and Table 1). Following the infusion, plasma growth hormone levels decreased gradually to preinfusion levels. Plasma growth hormone rose slightly but significantly only at 45 minutes after the onset of the infusion in the subjects receiving 50 mg/kg of arginine HCl, and did not rise in the individuals receiving 10 mg/kg of this compound (Table 1).

Plasma glucagon concentrations increased within 15 minutes of infusion in both the growth hormone–deficient patients and in the normal subjects who received either 500 or 200 mg/kg of arginine HCl and fell gradually back to baseline after the infusion. Plasma glucagon did not increase significantly in the subjects who received 50 mg/kg or 10 mg/kg of arginine HCl (Table 1).

The maximum plasma osmolality was observed at the end of the infusion (Table 1). In the growth hormone deficient and normal individuals receiving arginine HCl, 500 mg/kg, the rise in plasma osmolality was 9 ± 3 and 11 ± 5 mOsm/kg, respectively. After the infusion, osmolality fell progressively to baseline. There was no significant increase in plasma osmolality in the individuals receiving lesser quantities of arginine.

Since it is possible that a rise in plasma osmolality and blood volume induced by the arginine infusion caused the increase in ERPF and GFR, a control group of five normal subjects was infused for 30 minutes with 1000 mg/kg of D-glucose monohydrate or 60 g, whichever was less. This infusion increased plasma osmolality to 11 ± 4 mOsm/kg, which was similar to the rise in the normal and growth hormone deficient subjects who received 500 mg/kg of arginine HCl (Table 1). However, the maximum increase in ERPF and GFR after D-glucose infusion was only 11.2 ± 7.2% ($P < 0.05$) and 8.7 ± 8.4% (P : NS), respectively, (Table 1, Fig. 3). This increase in ERPF and GFR was significantly less than in the normal individuals infused with either 500 or 200 mg/kg of arginine HCl (at each dose of arginine infused, $P < 0.05$ for ERPF and $P < 0.05$ for GFR) and in the growth hormone–deficient patients ($P < 0.05$ for each comparison).

During the glucose infusion, when the ERPF rose and the GFR tended to increase there was no associated elevation in plasma growth hormone or glucagon (Fig. 3). However, plasma growth hormone increased significantly between three and four hours after the onset of the infusion to a maximum value of 11.2 ± 5.8 ng/ml. ERPF and GFR were not elevated above baseline at this time.

The infusion of 70 mmol ammonium chloride with 70 mmol sodium chloride in 300 ml water was carried out to assess whether the chloride load without arginine might increase ERPF and GFR. There was no change in either ERPF or GFR with this infusion (Table 1). The plasma osmolality rose by 8 ± 2 mOsm/kg (Table 1), which was of about the same magnitude and not significantly different from the increase in the normal and growth hormone–deficient patients given 500 mg/kg of

Table 1. Response of renal function and plasma hormones and osmolality to arginine or glucose infusion

Group	No. of subjects studied	Infusate	Dose *mg/kg*	Effective renal plasma flow *(ml/min/1.73m²* Base line	Minutes 0–30	30–60	90–120[a]	Glomerular filtration rate *ml/min/1.73m²* Base line	Minutes 0–30	30–60	90–120
GH Deficient	6	Arginine HCl	500	436[b] ±86	631[e] ±95	492 ±115	464 ±118	81 ±17	111[f] ±11	88 ±18	84 ±22
Normal	8	Arginine HCl	500	486 ±70	623[e] ±77	435 ±96	498 ±107	100 ±10	124[d] ±15	96 ±16	105 ±24
Normal	4	Arginine HCl	200	475 ±73	611[d] ±188	460 ±41	468 ±91	104 ±12	125[d] ±14	90 ±9	97 ±17
Normal	3	Arginine HCl	50	528 ±102	512 ±96	483 ±101	507 ±96	102 ±5	102 ±6	96 ±15	100 ±18
Normal	3	Arginine HCl	10	513 ±91	499 ±76	475 ±98	504 ±99	102 ±6	99 ±7	95 ±2	96 ±11
Normal	5	Glucose monohydrate	1000	523 ±63	584[d] ±95	502 ±94	507 ±129	99 ±13	108 ±16	95 ±17	100 ±18
Normal	5	NH_4Cl + NaCl	see below[c]	494 ±38	478 ±83	472 ±51	488 ±64	105 ±5	103 ±9	104 ±7	106 ±4

[a] Indicates duration of time in minutes after the onset of the respective 30 minute infusion.
[b] Values are expressed as mean ± SD.
[c] Each individual received 70 mmol of NH_4Cl with 70 mmol of NaCl in 300 ml water.
Significantly different from baseline values, [d] $P < 0.05$, [e] $P < 0.01$, [f] $P < 0.001$.

Table 1. *(Continued)*

Plasma growth hormone *mg/ml* Base line	Minutes 30	45	60	120	Plasma glucagon *pg/ml* Base line	Minutes 30	45	60	120	Plasma osmolality *mosm/kg* Base line	Minutes 30	45	60	240
0.5 ±0.1	0.7 ±0.3	0.8 ±0.3	0.8 ±0.3	0.7 ±0.3	177 ±83	663[f] ±202	485[e] ±236	388 ±138	203 ±82	274 ±7	283[d] ±10	281 ±10	278 ±10	275 ±6
0.8 ±0.8	11.3[d] ±11.0	24.0[e] ±19.1	23.5[e] ±16.9	8.2[d] ±10.5	181 ±63	678[f] ±209	572[e] ±193	408[d] ±205	224 ±69	278 ±4	289[f] ±5	283 ±7	283 ±6	282 ±7
1.1 ±1.2	6.5[d] ±5.7	13.2[e] ±11.7	13.8[d] ±16.6	2.6 ±2.3	145 ±16	359[f] ±76	190[e] ±49	159 ±39	118 ±56	279 ±6	282 ±6	280 ±6	280 ±4	274 ±6
0.5 ±0.0	4.3 ±6.5	4.4[d] ±6.8	2.1 ±2.6	0.7 ±0.2	158 ±7	193 ±60	119 ±10	129 ±20	146 ±28	273 ±1	275 ±1	274 ±2	273 ±2	275 ±3
7.9 ±6.7	4.3 ±4.2	2.3 ±2.2	1.4 ±1.1	1.0 ±0.3	143 ±53	117 ±64	119 ±44	113 ±66	113 ±44	280 ±2	279 ±2	281 ±3	282 ±2	279 ±2
1.6 ±1.3	2.6 ±3.5	2.5 ±3.4	1.2 ±0.4	1.3 ±0.6	165 ±80	122 ±92	129 ±91	136 ±111	200 ±129	285 ±3	296[e] ±4	292 ±4	287 ±6	285 ±4
										281 ±3	289[e] ±4	284 ±4	280 ±1	281 ±3

arginine HCl. Moreover, the rise in plasma osmolality with the ammonium and sodium chloride infusion was greater than with the 200 mg/kg of arginine HCl infusion ($P < 0.05$), where there was no significant change in plasma osmolality (+ 3 ± 4 mOsm/kg).

The fractional excretion of sodium rose in the growth hormone–deficient patients and the normal subjects infused with 500 or 200 mg/kg of arginine HCl (Fig. 4). The rise was most dramatic in the growth hormone–deficient patients, where the fractional sodium excretion increased from 1.78 ± 0.89% during baseline to a maximum value of 5.30 ± 2.72% which occurred one hour after the onset of the arginine infusion. The rise in the normal subjects given 500 or 200 mg/kg of arginine HCl was more gradual, and the maximum increase, which was less marked, occurred four or four and one–half hours after the end of the infusion (Fig. 4).

Discussion

This study was carried because of previous reports that in man and several animals an oral protein load or intravenous infusion of amino acids causes a rapid but transient increase in RPF and GFR [2–4]. Peptide hormones have been suggested as a cause of this response because somatostatin, which blocks the secretion of these hormones, also prevents the amino acid induced rise in RPF and GFR [4]. Both growth hormone and glucagon have been implicated [4, 7, 9].

We tested the hypothesis that either the presence of normal plasma growth hormone concentrations or a rise in plasma growth hormone–levels is necessary for the amino acid induced rise in RPF and GFR. L-arginine HCl, a potent secretogogue of growth hormone [12], was infused into both normal and growth hormone–deficient subjects. Both groups exhibited a substantial and transient increase in RPF and GFR, which was similar in magnitude to the rise after an oral protein load or mixed amino acid infusion in humans [4, 9]. The finding that plasma growth hormone was very low and did not increase during the arginine infusion and increased mainly after the infusion only in the normal subjects indicates that growth hormone did not mediate the arginine induced rise in RPF and GFR.

Other findings in this study also suggest that growth hormone

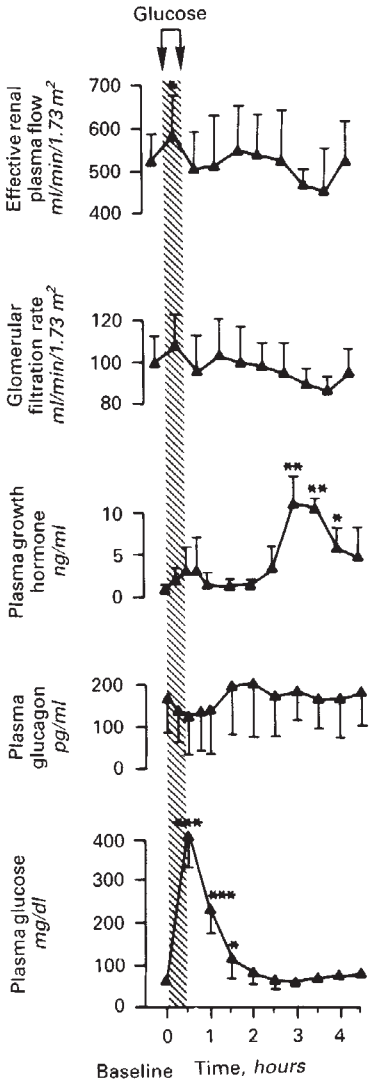

Fig. 3. *ERPF, GFR, plasma growth hormone, glucagon and glucose levels in normal subjects infused with D-glucose.* Significantly greater than baseline or pre-infusion values: $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$.

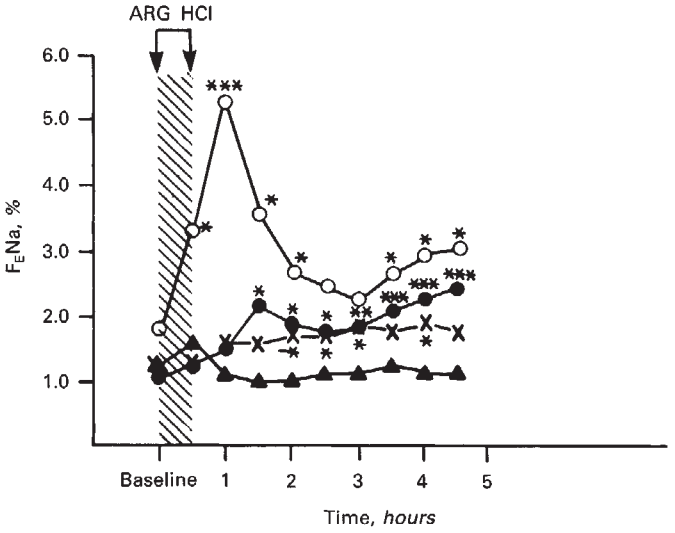

Fig. 4. *Fractional excretion of sodium in response to an infusion of arginine HCl or glucose in growth hormone deficient and normal subjects.* Significantly greater than baseline values: $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$.

does not play a role in the amino acid–induced acute rise in RPF and GFR. First, in the normal subjects, the maximum rise in growth hormone occurred after the rise in RPF and GFR. However, this discrepancy could be explained by an all or none response whereby when a certain plasma hormone level is attained, a maximal response is elicited and an additional increase in hormone stimulates no further response. Second, in the normal individuals who were infused with D-glucose, there was a small increase in RPF during the infusion even though plasma growth hormone–levels did not change. Third, in these same individuals, there was a delayed, approximately ninefold increase in plasma growth hormone–levels. This rise was approximately of the same magnitude as that observed in our normal subjects infused with 200 mg/kg of arginine HCl. However, in the individuals given D-glucose, the rise in plasma growth hormone was associated with, if anything, a tendency for RPF and GFR to fall.

Since the plasma arginine concentrations rose greatly with the 500 mg/kg dose, to 8055 ± 2191 and 13963 ± 7404 μmol/liter in the normal and growth hormone–deficient subjects, we studied the response to lower doses of arginine HCl in the normal individuals. The purpose of this study was to evaluate the effect on growth hormone and renal function of an amino acid load that was more physiological. When 200 mg/kg of arginine HCl was administered, the maximum rise in plasma arginine values, to 2342 ± 1527 μmol/liter, was similar to the total increase in plasma amino acids that occurs after a protein meal. Although plasma growth hormone and glucagon rose somewhat less with this infusion, the increment in RPF and GFR was similar to that of the normal individuals given 500 mg/kg of arginine HCl. Infusions of lower doses of arginine HCl, 50 and 10 mg/kg, were carried out in normal subjects to assess whether RPF and GFR would increase in the absence of a rise in growth hormone. We were unable to demonstrate such an effect, and so these studies were not continued.

The lower doses of arginine were also infused to investigate the possibility that the 500 mg/kg dose of arginine HCl increased RPF and GFR by an osmotic effect that increased plasma volume. The finding that, in the normal individuals given 200 mg/kg of arginine HCl, there was an increase in RPF and GFR but not in plasma osmolality suggests that an increase in plasma volume was not a major cause of the increase in renal function. This same issue was examined by infusing the D-glucose solution in a volume of water equal to the 500 mg/kg arginine HCl infusion. In this study, the osmolality increased to the same degree as in the normal and growth hormone–deficient subjects who received 500 mg/kg of arginine HCl. The ERPF, however, rose much less, and the GFR did not rise significantly. A small rise in ERPF and GFR with D-glucose infusion has been observed previously in humans and rats [3, 13]. These observations that osmotic and volume loads do not have a major effect on RPF and GFR has been reported by Meyer and Brenner [3].

The ammonium chloride and sodium chloride solution provided the same osmolar and chloride load as the 500 mg/kg

arginine HCl infusion. The finding that there was no change in ERPF and GFR with the former infusion indicates that neither, the osmolar nor the chloride load can account for the increase in renal hemodynamics with the arginine infusion.

Several investigators have implicated tubuloglomerular feedback as a mechanism contributing to the amino acid or protein induced increase in GFR [14–17]. However, during infusion of 500 mg/kg or 200 mg/kg of arginine HCl, the fractional excretion of sodium increased in the growth hormone deficient and normal subjects. These findings, although not conclusive, would suggest that the arginine HCl infusion, if it had any effect on tubuloglomerular feedback, would stimulate it to reduce the GFR. It is therefore unlikely that this mechanism could account for the arginine HCL-induced rise in RPF and GFR.

The results of the present study suggest that growth hormone does not mediate the acute amino acid–induced rise in RPF and GFR.

The finding of Kleinman and Glassock that after a large protein meal, GFR increased in all normal individuals but not in growth hormone–deficient subjects is puzzling [9]. However, plasma growth hormone rose in only one of their four normal subjects. This also indicates that an increase in plasma growth hormone is not necessary for the acute rise in GFR after the protein load. The authors conclude that a pituitary–hypothalamic disorder, other than the growth hormone deficiency, may be responsible for the failure of GFR to increase in the growth hormone–deficient patients [9].

Parving and associates observed no increase in RPF or GFR in normal individuals who were infused with growth hormone for two hours [18]. The finding that growth hormone injections for several days increased RPF and GFR suggests that persistent or recurrent elevations of this hormone could increase RPF and GFR [6, 7]. Serum somatomedin levels may not increase until many hours after plasma growth hormone rises [19]. Hence, the finding that a rise in plasma growth hormone for several days causes a delayed increase in RPF and GFR may indicate that these latter efffects are mediated by somatomedins.

In the present study, the rise and peak values of plasma glucagon after the infusion of 500 mg/kg or 200 mg/kg of arginine HCl occurred at the same time that RPF and GFR increased in the normal and growth hormone–deficient subjects. These findings are consistent with the observations by other workers that an infusion of glucagon in dogs or humans can acutely increase RPF and GFR [20–23].

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Reprint requests to Joel D. Kopple, M.D., Division of Nephrology and Hypertension, Harbor-UCLA Medical Center, 1000 Carson St., Torrance, California 90509, USA.

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